

23



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,385	07/06/2001	Joyce A. Deleo	DC-0156	4729
26259	7590	02/13/2006	EXAMINER	
LICATLA & TYRRELL P.C. 66 E. MAIN STREET MARLTON, NJ 08053			JAGOE, DONNA A	
			ART UNIT	PAPER NUMBER

1614

DATE MAILED: 02/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/857,385	<b>Applicant(s)</b> DELEO ET AL.	
	<b>Examiner</b> Donna Jagoe	<b>Art Unit</b> 1614	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 17 October 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

Art Unit: 1614

***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 17 October 2005 has been entered.

Claim 1 is pending in this application.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that

Art Unit: 1614

the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chamberlain et al. (Archives of Neurology).

The claim is drawn to a method of treating lower back pain with radiculopathy to an animal in need of treatment consisting of locally administering methotrexate intrathecally to the back of said animal at doses below 3mg/kg so that lower back pain with radiculopathy is reduced.

Chamberlain et al. teach administration of methotrexate to patients with leptomeningeal metastases presenting with radiculopathy (see abstract). Methotrexate is administered intraventricularly in doses of 2 mg daily (total dose of 40 mg) (see page 508, column 1). Chamberlain et al. teach the same composition of methotrexate in the same dose (less than 3mg/kg) to be useful in treatment of leptomeningeal metastases with radiculopathy.

The prior art differs in that it does not teach intrathecal administration to the back. However Chamberlain et al. teach intraventricular administration. The definition of intrathecal administration from Stedman's Medical Dictionary, 27<sup>th</sup> edition is administration within either the subarachnoid or the subdural space. Since the

Art Unit: 1614

method of administering an agent intrathecally can mean that the agent is administered into the subarachnoid or subdural space, the method of administering intrathecally overlaps with Chamberlain's method of administering intraventricularly to treat leptomeningeal metastases with radiculopathy.

Applicant has added the limitation that the injection site is the back of said animal. However, since the exact sight of the back is unknown it is unclear whether the injection site is on back of the animal or the back of the head (subdural space). As such, it appears that there is overlap between the methotrexate injection of Chamberlain et al. and the instant invention. Although the prior art administers methotrexate for treatment of leptomeningeal metastasis, it provides relief of the symptoms, such as radiculopathy, and as such, it is reasonable and self-evident that methotrexate must treat the radiculopathy in each case, whether explicitly recognized or not. It would have been made obvious to one of ordinary skill in art at the time it was made to administer methotrexate in a dose below 3 mg/kg to reduce lower back pain with radiculopathy motivated by the teaching of Chamberlain et al. who teaches that methotrexate is effective at a dose of 2mg/kg administered intraventricularly to treat leptomeningeal metastasis with radiculopathy.

### ***Response to Arguments***

Applicant asserts that the dose of methotrexate administered intraventricularly would result in only a small amount of circulation of the injected drug, via the cerebrospinal fluid, into the spinal cord, the concentration of

Art Unit: 1614

methotrexate achieved would not be expected by one of skill in the art to be as high as could be achieved through direct administration into the spinal cord area via intrathecal administration since the only some of the cerebrospinal fluid is circulated from the ventricles into the central canal of the spinal cord. Applicant cites Human Anatomy and Physiology, Second Edition pages 404-405 as evidence of this assertion. In response, the examiner points to the dosage of methotrexate recited in line 4 of the instant claim. The amount claimed is "below 3 mg/kg". This can mean 0 mg/kg and as such, even if none of the methotrexate reaches the spinal cord, the intraventricular administration of methotrexate of Chamberlain et al. meets the claim.

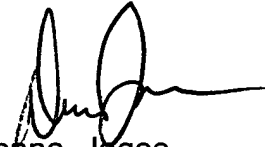
### ***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Thursday from 9:00 A.M. - 3:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

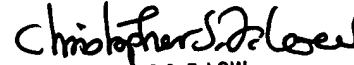
Art Unit: 1614

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Donna Jagoe  
Patent Examiner  
Art Unit 1614

February 2, 2006



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